IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of separating an immunoreactive compound from at least one immaterial component in a fluid mixture using simulated moving bed (SMB) affinity chromatography which comprises the steps of: (a) providing a simulated moving bed apparatus that comprises a plurality of modules in fluid conducting communication, said modules comprising at least one solid phase comprising a ligand for which the immunoreactive compound has selective affinity; (b) continuously introducing the fluid mixture into said simulated moving bed apparatus wherein the fluid mixture contacts the solid phase in a countercurrent mode; (c) effecting separation of the immunoreactive compound from at least one immaterial component; ~~and~~ (d) collecting the immunoreactive compound to provide a purified composition thereof; and (e) regenerating the at least one solid phase of step (a).

2. (Canceled)

3. (Currently amended) A method according to claim ~~2~~ 1 wherein the immunoreactive compound associates with the solid phase to a greater degree than at least one immaterial component.

4. (Currently amended) A method according to claim 3 which further comprises the step of effecting said separation by contacting said solid phase with an eluent that promotes disassociation of the immunoreactive compound from the solid phase.

5. (Currently amended) A method according to claim 4 wherein the immunoreactive compound comprises a constant region of an immunoglobulin, and said solid phase comprises a support material associated with Protein A or Protein G.

6. (Original) A method according to claim 5 wherein said eluent comprises an acidic buffer.

7-30. (Canceled)

31. (New) A method according to claim 1, wherein the immunoreactive compound is selected from the group consisting of an antibody, an antibody fragment, a domain-deleted antibody, an antibody linked to a moiety capable of binding specifically to another molecule, and a fusion protein comprising a region of an immunoglobulin polypeptide fused to a polypeptide capable of specific binding to a ligand.

32. (New) A method according to claim 5, wherein the immunoreactive compound comprises an antibody or an antibody fragment.

33. (New) A method according to claim 1, wherein the concentration of immunoreactive compound collected from the SMB apparatus in step (d) is greater than the concentration of immunoreactive compound in the fluid mixture that is introduced into the SMB apparatus in step (b).

34. (New) A method according to claim 1, wherein step (e) comprises contacting the solid phase with a regeneration buffer.

35. (New) A method according to claim 34, wherein the regeneration buffer comprises urea.

36. (New) A method according to claim 1, wherein step (e) comprises contacting the solid phase with a clean in place (CIP) solution.

37. (New) A method according to claim 36, wherein the CIP solution comprises phosphoric acid.

38. (New) A method according to claim 1, wherein step (b) comprises continuously introducing the fluid mixture comprising the immunoreactive compound and at least one immaterial component into a module in an association zone comprising the solid phase, wherein the fluid mixture contacts the solid phase in a countercurrent mode and the immunoreactive compound and at least one immaterial component differentially associate with the solid phase;

wherein step (c) comprises introducing a wash buffer into a module comprising the associated immunoreactive compound in at least one wash zone, whereby at least one immaterial component is dissociated from the solid phase and is substantially removed from the module;

and wherein step (d) comprises (i) introducing an eluent into a module comprising the associated immunoreactive compound in an elution zone, whereby the immunoreactive compound is dissociated from the solid phase and is removed from the module; and (ii) removing a product stream comprising the immunoreactive compound that is substantially separated from at least one immaterial component in said fluid mixture.

39. (New) A method according to claim 38, wherein effluent from a module in at least one wash zone is fed back into a module in the association zone.

40. (New) A method according to claim 38, wherein step (c) of said method comprises introducing a high salt wash buffer into a module comprising the associated immunoreactive compound in a first wash zone.

41. (New) A method according to claim 40, wherein step (c) of said method further comprises introducing a low salt wash buffer into a module comprising the associated immunoreactive compound in a second wash zone.

42. (New) A method according to claim 38, further comprising a step following wash step (c) that comprises introducing solution containing purified immunoreactive compound from the product stream into a module in an entrainment rejection zone prior to elution of immunoreactive compound from said module.

43. (New) A method according to claim 38, further comprising a step following elution in step (d) that comprises introducing elution wash buffer into a module in an elution wash zone.

44. (New) A method according to claim 38, wherein step (e) comprises introducing a regeneration buffer into a module comprising the at least one solid phase of step (a) in a regeneration zone.

45. (New) A method according to claim 44, wherein the regeneration buffer comprises urea.

46. (New) A method according to claim 38, wherein step (e) comprises contacting the at least one solid phase of step (a) with a CIP solution.

47. (New) A method according to claim 46, wherein the CIP solution comprises phosphoric acid.

48. (New) A method according to claim 38, further comprising a step prior to introducing the fluid mixture into the module in step (b) that comprises introducing a re-equilibration buffer into a module comprising the solid phase in a re-equilibration zone, wherein the re-equilibration buffer creates an environment in the module that permits binding of the immunoreactive compound to said ligand.

49. (New) A method according to claim 38, wherein the immunoreactive compound is selected from the group consisting of an antibody, an antibody fragment, a domain-deleted antibody, an antibody linked to a moiety capable of specific binding to a ligand, and a fusion protein comprising a region of an immunoglobulin polypeptide fused to a polypeptide capable of specific binding to a ligand.

50. (New) A method according to claim 38, wherein the immunoreactive compound comprises a constant region of an immunoglobulin, and the at least one solid phase of step (a) comprises Protein A or Protein G.

51. (New) A method according to claim 38, wherein the concentration of immunoreactive compound in the product stream is greater than the concentration of immunoreactive compound in the fluid mixture that is introduced into a module in the association zone in step (b).

52. (New) A method of separating an immunoreactive compound from at least one immaterial component in a fluid mixture using SMB affinity chromatography, comprising:

(a) providing a SMB apparatus that comprises at least one module in fluid conducting communication with said apparatus, wherein said module comprises at least one solid phase comprising a ligand for which the immunoreactive compound has selective affinity, and wherein said apparatus comprises a plurality of zones through which the module passes;

(b) introducing the fluid mixture into the module in an association zone wherein the fluid mixture contacts the solid phase in a countercurrent mode and the immunoreactive compound associates with the solid phase;

(c) introducing a wash buffer into the module comprising the associated immunoreactive compound in at least one wash zone, wherein the wash buffer contacts the solid phase and substantially removes at least one immaterial component from said module;

(d) introducing an eluent into the module comprising the associated immunoreactive compound in an elution zone, wherein the eluent contacts the solid phase and promotes disassociation of the immunoreactive compound from the solid phase;

(e) removing a product stream comprising the immunoreactive compound that is substantially separated from at least one immaterial component in said fluid mixture;

(f) introducing a re-equilibration buffer into the module in a re-equilibration zone, wherein the re-equilibration buffer creates an environment in the module that permits binding of the immunoreactive compound to the solid phase comprising the ligand.

53. (New) A method according to claim 52, further comprising regenerating the at least one solid phase of step (a).

54. (New) A method according to claim 53, which comprises introducing a regeneration buffer into a module comprising the at least one solid phase of step (a) in a regeneration zone.

55. (New) A method according to claim 54, wherein the regeneration buffer comprises urea.

56. (New) A method according to claim 53, which comprises contacting the at least one solid phase of step (a) with a CIP solution.

57. (New) A method according to claim 56, wherein the CIP solution comprises phosphoric acid.

58. (New) A method according to claim 52, wherein the SMB apparatus comprises a plurality of modules.

59. (New) A method according to claim 52, wherein the immunoreactive compound is selected from the group consisting of an antibody, an antibody fragment, a domain-deleted antibody, an antibody linked to a moiety capable of binding specifically to another molecule, and a fusion protein comprising a region of an immunoglobulin polypeptide fused to a polypeptide capable of specific binding to a ligand.

60. (New) A method according to claim 52, wherein the immunoreactive compound comprises a constant region of an immunoglobulin and the solid phase comprises Protein A or Protein G.

61. (New) A method according to claim 60, wherein the eluent comprises an acidic buffer.

62. (New) A method according to claim 52, wherein effluent of a module in at least one wash zone is fed back into a module in the association zone.

63. (New) A method according to claim 52, wherein step (c) of said method comprises introducing a high salt wash buffer into a module comprising the associated immunoreactive compound in a first wash zone.

64. (New) A method according to claim 63, wherein step (c) of said method further comprises introducing a low salt wash buffer into a module comprising the associated immunoreactive compound in a second wash zone.

65. (New) A method according to claim 52, further comprising a step following wash step (c) that comprises introducing solution containing purified immunoreactive compound from the product stream into a module in an entrainment rejection zone prior to elution of immunoreactive compound from said module.

66. (New) A method according to claim 52, further comprising a step following elution in step (d) that comprises introducing elution wash buffer into a module in an elution wash zone.

67. (New) A method according to claim 52, wherein the concentration of immunoreactive compound in the product stream obtained in step (e) is greater than the concentration of immunoreactive compound in the fluid mixture that is introduced in step (a).